Original Article

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Do TSH Levels in Euthyroid Patients have an Impact on the Prevalence of Metabolic Syndrome

Ötiroid Hastalarda TSH Düzeyi Metabolik Sendrom Sıklığını Etkiler mi?

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Abstract

Purpose: Our objective in this study was to investigate the prevalence of metabolic syndrome in two different group of patients who had a thyroid-stimulating hormone (TSH) level within normal limits.

Material and Method: Three hundred and fifty patients, who presented to Aksaray Public Hospital, Endocrinology and Metabolism Diseases Outpatient clinic and who had no thyroid disease, were included in the study. The patients were divided into two groups according to TSH levels. Group 1 had a TSH level of <2.5 mIU/L and group 2 had a TSH level of >2.5 mIU/L. The prevalence of metabolic syndrome, insulin resistance and lipid parameters were investigated in both groups.

Results: A total of 350 patients were included in the study. Group 1 included 229 (65.5%) patients and group 2 included 121 (34.5%) patients. The prevalence of metabolic syndrome was found to be 112/229 (48%) in group 1 and 55/121 (45%) in group 2. There was no statistically significant difference between the two groups (p>0.05). FT3 level was found to be positively correlated with hip circumference (r=0.10, p=0.04), weight (r=0.12; p=0.016) and waist circumference (r=0.13; p=0.014). FT4 level was found to be positively correlated with height (r=0.12, p=0.02).

Discussion: TSH level was not found to be correlated with the prevalence of metabolic syndrome (p>0.05). The prevalence of metabolic syndrome was found to be similar in both groups. *Turk Jem 2015; 19: 34-37*

Key words: Metabolic syndrome, TSH, thyroid

Conflicts of Interest: The authors reported no conflict of interest related to this article.

Özet

Amaç: Bu çalışmadaki amacımız tiroid stimulan hormon (TSH) düzeyi normal sınırda ve birbirinden farklı iki grupta metabolik sendrom sıklığını araştırmaktır.

Gereç ve Yöntem: Aksaray Devlet Hastanesi Endokrinoloji ve Metabolizma Hastalıkları polikliniğine başvuran tiroid hastalığı olmayan 350 hasta çalışmaya alındı. Hastalar TSH düzeylerine göre iki gruba ayrıldı. Grup 1: TSH <2,5 IU/dl ve grup 2: TSH >2,5 IU/dl olarak ayrıldı. Her iki grupta metabolik sendrom sıklığı, insülin direnci, lipid parametreleri araştırıldı.

Bulgular: Çalışmaya toplam 350 hasta alındı. Grup 1'de 229 (%65,5) hasta, grup 2'de 121 (%34,5) hasta vardı. Grup 1'de metabolik sendrom sıklığı 112/229 (%48), grup 2'de metabolik sendrom sıklığı 55/121 (%45) olarak tesbit edildi. İki grup arasında anlamlı istatistiksel fark yoktu (p>0,05). ST3 düzeyi kalça çevresi (r=0,10, p=0,04), kilo (r=0,12, p=0,016) ve BÇ (r=0,13, p=0,014) ile pozitif korele bulundu. sT4 düzeyi boy ile pozitif korele (r=0,12, p=0,02) bulundu.

Tartışma: TSH düzeyi metabolik sendrom sıklığı ile korele bulunmadı (p>0,05). Her iki grupta metabolik sendrom sıklığı benzer bulundu. *Turk Jem 2015; 19: 34-37*

Anahtar kelimeler: Metabolik sendrom, TSH, tiroid

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Introduction

Metabolic syndrome (MS) is a fatal endocrinopathy which starts with insulin resistance (IR) in which abdominal obesity, glucose intolerance or systemic disorders including diabetes mellitus, dyslipidemia, hypertension and coronary artery disease (CAD) are added to each other (1). The prevalence of MS in our country is 28% in men and 40% in women which are considerably high values. In our country, the prevalence of MS was found to be 35% in adults aged 20 years and above according to the results of METSAR (Turkey Metabolic Syndrome Investigation) performed in 2004. In this study, the prevalence of MS was found to be higher in women compared to men (41.1% in women, 28.8% in men) (2). Thyroid hormones have many effects on energy homeostasis, lipid and glucose metabolism as well as blood pressure. Thus, the hypothesis that altered thyroid functions may be related with MS and its components has been proposed (3). It has been proposed that some hormonal and humoral mediators stimulate the hypothalamic-pituitary-thyroid (H-P-T) axis and increase secretion of thyroid-stimulating hormone (TSH) (4). It has been shown that the components of MS and IR are significantly related with decreased free T4 (fT4) and/or increased TSH levels within the euthyroid limits. The main suspected mechanism is the potential relationship between leptin and thyroid hormones (5,6,7,8). In a study conducted with euthyroid premenopausal women, the prevalence of MS was found to be higher in the group with TSH levels of >2.5 than in low-TSH group (9). Our objective in this study was to investigate thyroid functions, IR, serum lipid and MS components in euthyroid patients as well as the effect of increased TSH levels on the prevalence of metabolic syndrome.

Materials and Methods

Three hundred and fifty euthyroid patients aged between 18 and 65 years, who presented to Aksaray Public Hospital, Endocrinology Outpatient clinic between January 2013 and December 2013, were included in the study. The patients were divided into two groups as group 1 (TSH <2.5 mIU/L) and group 2 (TSH >2.5 mIU/L). In both groups, euthyroidism was defined as TSH (0.35-4.0 mIU/L), fT3 (1.71-4.71 pg/ml) and fT4 (0.8-1.9 ng/ml) levels within normal reference limits.

MS was determined according to National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria (1). Accordingly, a diagnosis of MS was made, when at least 3 of the 5 diagnostic criteria [increased fasting plasma glucose level (>110 mg/dl), visceral obesity (waist circumference >88 cm in women and >102 cm in men), hypertension (>130/85 mmHg), hypertriglyceridemia (≥150 mg/dl), and decreased HDL cholesterol (<40 mg/dl in men, <50 mg/dl in women)] were present (1). Study exclusion criteria included a history of thyroid disease, previous levothyroxine treatment, high antibody levels and a history of neck radiation and thyroidectomy.

Antropometric Measurements

Medical history was taken and physical examination was performed in all patients included in the two groups before starting the study. Blood pressure was measured with the same sphygmomanometer in fasting state and after a rest period of at least 10 minutes for 2 times with an interval of 3 minutes and the average of the measurements was taken. Height was measured with a standard medical study meter and body weight was measured with a standard medical scale. Waist circumference (WC) was measured with a tape measure. WC of the patients was measured after removing clothing at the most indented site between the 10th rib and the iliac crest in the middle of respiration. Body mass index (BMI) was calculated separately for each subject as weight (kg)/height^2 (m^2).

Laboratory Analyses

After a fasting period of 12 hours, venous blood samples were taken between 8:00 and 9:00 hours in the morning and fasting blood glucose (FBG), insulin, LDL-C, TG, fT3, fT4 and TSH levels were measured. IR was measured according to the Homeostasis Model Assessment (HOMA) system defined by Matthews et al. as follows: HOMA-IR= [fasting plasma insulin (IU/ml) x fasting plasma glucose (mmol/L)] /22.5 (10). A HOMA-IR value of >2.7 was considered IR (11).

Serum glucose level was measured using the glucose oxidase technique (Roche Diagnostics GmhB, Manheim, Germany). HDL-C, LDL-C and TG levels were measured by direct quantitative analysis using enzymatic methods with Hitachi Modular System (Roche Diagnostics GmhB) device of the German company named Roche Molecular Biochemicals Manheim. Serum insulin levels were measured by solid-phase competitive chemiluminescent enzyme immunoassay (Bio- DPC Diagnostic products Corporation Los Angeles, USA, Immulite 2000). fT3, fT4 and TSH levels were measured with automated analyzer using immunochemiluminescent method (Bio-DPC Diagnostic products Corporation Los Angeles, USA, Immulite 2000).

Statistical Assessment

Statistical analyses were performed using SPSS version 17.0 (Statistical Package for the Social Sciences, version 17.0, SSPS Inc. Chicago). The demographic data of the study were evaluated by frequency analyses, median, mean and standard deviation values. Numerical data were evaluated using chi-square and student's t-tests. Pearson's correlation coefficient was used for correlation analyses. In all assessments, a p value of less than 0.05 was considered statistically significant in a confidence interval of 95%.

Results

The general properties of the patients included in the study are shown in Table 1. A total of 350 patients were included in the study. The mean age and BMI, FBG, insulin, HOMA-IR, and TSH levels were 38.94±11.7 years, 31±6.1, 94.7±11.7 mg/dl, 11.5±5.8, 2.7±1.47, 2.2±1.2 mmol/l, respectively (Table 1). There was a negative correlation between TSH levels and age (r=0.13, p=0.011). The patients were divided into two groups according to TSH levels. Group 1 (TSH <2.5) included 229 (65.5%) patients and group 2 (TSH >2.5) included 121 (34,5%) patients. 308 patients were female (88%) and 42 (12%) were male. Group 1 included 196 female patients and 33 male patients, while group 2 included 112 female patients and 9 male patients. WC, BMI, FBG, insulin, blood pressure,

HOMA-IR and total cholesterol, LDL-C, HDL-C,TG levels were found to be similar in the two groups (p>0.05) (Table 2). The prevalence of MS was found to be 48% (112/229) according to NCEP ATPIII criteria and %54 (125/229) according to the International Diabetes Federation (IDF) 2007 in group 1 and 45% (55/121) according to the NCEP ATP III criteria, and 49% (60/121) according to the IDF 2007 in group 2. There was no statistically significant difference between the two groups (p>0.05). In group 1, the mean fT3, fT4 and TSH levels were found to be 4.62±19.6, 1.18±0.24 and 1.42±0.61, respectively. In group 2, the mean fT3, fT4 and TSH levels were 2.86±0.45, 1.18±0.24 and 3.85±1.10, respectively. There was no statistically significant difference between the groups in terms of fT3 and fT4 levels. The TSH value was statistically significantly higher group 2 than group 1 (p<0.0001). fT3 level was found to be positively correlated with hip circumference (r=0.10, p=0.04), body weight (r=0.12, p=0.016) and WC (r=0.13, p=0.014). fT4 level was found to be positively correlated with height (r=0.12, p=0.02). The prevalence of MS in the groups are shown in Table 3. MS components were found to be similar in both groups.

Table 1. Metabolic charecterisrics of the subjects

Variable	Value	Normal range
Number	350	
Age (years)	38.94±11.7 (16-78)	
BMI (kg/m^2)	31.0±6.1 (18-51)	
WC (cm)	94.3±15.3 (60-147)	
FBG (mg/dl)	94.7±11.7 (70-188)	70-100 mg/dl
Insulin (iu/ml)	11.5±5.8 (2-39)	
HOMA-IR	2.7±1.47 (0,4-8.99	
Systolic BP (mm-Hg)	117.0±17.9 (90-180)	
Diastolic BP (mm-Hg)	70.9±10.8 (50-120)	
T.Chol. (mg/dl)	197.0±40.7 (95-343)	120-200 mg/dl
TG (mg/dl)	149.8±72.8 (43-459)	0-200 mg/dl
HDL-C (mg/dl)	45.8±11.8 (16-61)	35-55 mg/dl
LDL-C (mg/dl)	122.2±35.8 (53-290)	50-130 mg/dl
TSH (mmol/l)	2.2±1.2 (0.14-5.7)	0.27-4.20 (mmol/l)
sT3 (mmol/l)	2.8±0.48 (0.98-3.99)	2-4.4 mmol/l
sT4 (mmol/l)	1.15±0.2 (0.78-2.80)	0.93-1.70 mmol/l

Table 2. General properties of the groups

	Group 1 (n=229)	Group 2 (n=121)	p	Normal range
Age (years)	39.8±11.3	37.3±12.5	0.65	
Height (cm)	162.0±7.5	160.6±9.9	0.13	
Weight (kg)	81.5±17.1	81.1±18.7	0.82	
BMI (kg/m^2)	31.0±6.2	32.0±12.7	0.3	
WC (cm)	94.4±14.8	94.4±16.2	0.85	
FBG (mg/dl)	95.4±10.8	93.5±13.2	0.14	70-100 mg/dl
Insulin (iu/ml)	2.7±1.5	2.6±1.3	0.53	
HOMA-IR	2.8±2.0	2.63±1.3	0.38	
Systolic BP (mm-Hg)	117.0±18.0	116.9±17.7	0.95	
Diastolic BP (mm-Hg)	71.1±11.3	70.4±10.1	0.57	
T.Chol. (mg/dl)	197.7±40.6	195.7±41.0	0.65	120-200 mg/dl
TG (mg/dl)	155.2±99.1	147.9±66.8	0.47	0-200 mg/dl
HDL-C (mg/dl)	45.5±11.7	46.3±12.0	0.56	35-55 mg/dl
LDL-C (mg/dl)	124.7±42.5	120.0±34.9	0.29	50-130 mg/dl
sT3 (mmol/l)	4.6±19.6	2.8±0.4	0.32	2-4.4 mmol/l
sT4 (mmol/l)	1.17±0.2	1.18±0.18	0.01	0.93-1.70 mmol/l
TSH (mmol/l)	1.42±0.61	3.85±1.1	0.0001	0.27-4.20 mmol/l

Discussion

In this study, we evaluated that the effect of increased TSH levels on metabolic syndrome, IR and lipid parameters in 350 healthy patients aged between 18 and 65 years. MS is an endocrinopathy which starts with IR in which abdominal obesity, glucose intolerance or systemic disorders including diabetes mellitus, dyslipidemia, hypertension and coronary artery disease are added to each other and which causes extensive mortality and morbidity. It is known that thyroid hormones have many effects on energy homeostasis, lipid and glucose metabolism and blood pressure (12). It has been proposed that there may be a relationship between thyroid hormones and MS parameters. Currently, there are studies proposing that there may be a relationship between MS and/or IR and thyroid hormones. In our study, the relationship between thyroid functions and the components of MS was examined. There was no significant difference between the two groups in terms of the prevalence of MS. Increased TSH level within the normal limits did not affect the prevalence of MS. In a study in which patients with subclinical hypothyrodism and euthyroid patients were compared, no relationship could be found between the two groups in terms of the prevalence of MS (13). Decreased fT4 level was found to be correlated with glucose, HOMA-IR, and increased cholesterol values. In our study, fT4 level was found to be positively correlated with height. No correlation

Table 3. The prevalence of metabolic syndrome in the groups

Metabolic syndrome	Group 1 (n=229)	Group 2 (n=121)	Total
No	117 (51.09%)	66 (54.5%)	183
Yes	112 (48.9%)	55 (45.5%)	167
Total	229 (100%)	121 (100%)	350

Table 4. Hormon levels distribution of the metabolic syndrome and non metabolic syndrome groups

	Metabolic syndrome group n=167	Non-metabolic syndrome group n=183	p
sT3 (mmol/l)	2.9±0.50	2.9±0.45	0.243
sT4 (mmol/l)	1.16±0.25	1.16±0.21	0.921
TSH (mmol/l)	2.27±1.4	2.26±1.43	0.955

was found with the other parameters. In our study, the prevalence of MS was similar between the groups as according to TSH levels (p>0.05). In a study performed by Park et al., increased TSH levels within the normal limits increased the odds ratio of the prevalence of MS by 1.95 (14). In a study performed in Korea involving 2760 women aged between 18 and 39 years with a TSH level of (0.3-4.2 mU/L), the diagnosis of MS was made according to the 2007 International Diabetes Federation criteria and the prevalence of MS was found to be significantly higher in the group with a TSH level above 2.5 mU/L (7.5%, 4.8%, p=0.016). In the group with higher TSH level, the prevalence of MS was found to be 2-fold higher according to age and BMI (odds ratio: 1.9; 95% confidence interval, 1.1 to 3.2). (9). The ATP III criteria were used in our study and the prevalence of MS was found to be 45% in the group with higher TSH levels and 48% in the group with lower TSH levels. The difference between the two groups was not found to be significant (p>0.05). Based on the IDF 2007 criteria, there was no statistically significant difference in the prevalence of MS between the two groups (p>0.05). In their study performed in Turkey, Tarçın et al. compared 122 patients with MS with a group without MS and found higher fT4and fT3/fT4 ratio in the MS group (15). MS parameters (excluding HDL) were found to be correlated with TT3, fT4 and fT3/fT4 ratio. Different results regarding the relationship between obesity and serum free thyroid hormones have been reported in different studies. Accordingly, increased or decreased serum fT3 or fT4 concentrations have been found in obese patients (16). In MS group the mean fT3, fT4 and TSH levels were 2.9±0.5 mmol/l, 1.16±0.25 mmol/l and 2.27±1.4 mmol/l, respectively. (Table 4) In many studies, a relationship was found between low/normal fT4 levels in euthyroid limits in MS and lipid abnormalities and increased IR (6,8,12). In addition, it has been shown in previous studies that low/normal fT4 levels and/or increased TSH levels were significantly related with MS and its components (7,9,17). In a study performed in Korea, which included 7270 patients, TSH level was found to be correlated with gender, age, and BMI (in men). As the TSH level increased within the normal limits, the prevalence of MS increased (18). In another study, which included 1333 patients, TSH level was found to be poorly correlated with BMI (r=0.061, p=0.025). In patients with a TSH level in the upper limit (2.5-4.5 mU/l, n=119), BMI was found to be significantly increased (30.47+/-0.57 vs. 28.74 +/-0.18 kg/m$^{(2)}$, p=0.001), triglyceride was found to be significantly increased (1.583 +/-0.082 vs. 1.422 +/-0.024 mmol/l, p=0.023) and a 1.7-fold increase was found in the prevalence of MS according to the ATP III (95% CI: 1.11-2.60) (19). In our study, despite the increased TSH levels, there was no difference in the MS parameters between the groups. Our study's results was discordant with literature. The reason for this could include a small number of patients in our study. The larger case series will give more accurate results.

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